REMARKS

Applicants wish to thank the Examiner for reconsidering the status of the March 31, 2008 Office Action and for withdrawing its finality.

The Claim Amendments

Claim 47 has been amended to recite a pharmaceutical composition comprising a compound of formula **I**, wherein Ar^1 is an optionally substituted phenyl ring. Support for this amendment is found in paragraphs [0088] and [0091] on pages 31 and 33, respectively, of the specification.

Claim 50 has been amended to recite a method of inhibiting c-MET kinase activity in a biological sample with a compound of formula **I** or a composition comprising said compound, wherein Ar^1 is an optionally substituted phenyl ring, Support for this amendment is found in paragraphs [0088] and [0091] on pages 31 and 33, respectively, of the specification.

Claims 60, 86, and 95 have been canceled.

Claim 101 has been amended such that the scope of this claim corresponds to that of amended claim 47.

None of the amendments add new matter. Their entry is requested.

The Response

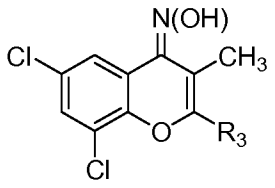
Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 47, 50, 60, 81, 83-90, 92-98, and 101 under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. In particular, the Examiner asserts that it is not clear what specific embodiments of the generically claimed formula would show useful biological activity. Claims 60, 86, and 95 have been canceled, thereby making the rejection of these claims moot. Applicants traverse in view of the amended claims.

Claims 47 and 50, and claims dependent thereon, have been amended such that they recite pharmaceutical compositions or methods comprising a compound of formula **I**, wherein Ar^1 is an optionally substituted phenyl ring. Compounds that inhibit c-Met activity with a K_i of less than or equal to 1 μM and that fall within the scope of the amended claims include compounds **I**-11, **I**-12, **I**-13, **I**-15, **I**-20, **I**-21, **I**-23, **I**-24, **I**-26, **I**-27, **I**-28, **I**-29, **I**-31, **I**-32, **I**-33, **I**-34, **I**-35, **I**-36, and **I**-37. See paragraph [00121] on pages 39-42 of the specification for the structures of these compounds. In the Reply to Office Action filed on May 16, 2007 (hereafter, "the May Reply"), applicants presented evidence that a link between c-Met kinase activity and various cancers was established at the time of the invention. Applicants have also presented evidence that a small molecule c-Met inhibitor was shown to have anti-tumor effects in an *in vivo* model. See the discussion presented in the May Reply relating to paragraphs [0048] to [0050] on pages 14-15 of the specification. Since compounds that are representative of the amended claims have the ability to inhibit c-Met activity in an *in vitro* assay and such inhibition is linked to useful *in vivo* biological activity, the present invention is enabled. Accordingly, applicants respectfully request that the Examiner withdraw the rejection of claims 47, 81, 83-85, 87-90, 92-94, 96-98, and 101 under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claim 47, 50, 60, 81, 83-90, 92-98, and 101 under 35 U.S.C. § 103(a) for allegedly being obvious over Moon et al., U.S. Patent No. 4,065,574 (hereafter "Moon"). In particular, the Examiner asserts that Moon teaches that compounds such as the following have anti-fungal activity:



, wherein R_3 is hydrogen.

Applicants traverse in view of the amended claims. Claims 60, 86, and 95 have been canceled, thereby making the rejection of these claims moot.

First, the compounds of Moon are not pharmaceutically useful compounds such as those of the instant invention, but are instead directed at preventing damage due to fungi in seeds, plants, animals, objects, or places. See the abstract of Moon. See also column 11, lines 25-28, of Moon which states: "[t]he novel formulations of the invention are used to kill and control fungi on organic matter such as wood, cellulosic fibers, leather, seeds, fruits, vegetables, living plants, and on various animals, for example, fishes, reptiles, birds, cattle, horses, dogs, and cats." Second, the Examiner has failed to fully ascertain the structural differences between the compounds of Moon and those of the present invention. In the compounds of Moon, the R_3 substituent is described as being hydrogen, halogen, hydroxyl, or lower alkyl. See column 1, lines 39-40, of Moon. In the compounds used in the compositions of the present invention, the substituent that corresponds to R_3 is an optionally substituted phenyl ring. Nothing in Moon provides a person skilled in the art any reason to prepare such phenyl-substituted compounds. In addition, the Examiner states that "one skilled in the art of medicinal chemistry would be motivated [by Moon] to assay the many known and structurally modified oximes … with similar structure (see references cited under § 102(b)) [from the December 27th Office Action]; the applicant deleted many oxime compounds known in the prior art to overcome the previously presented rejections under § 102(b) for biological activity…" (emphasis added). That was not the case. Compounds were not removed in the claim amendments for reasons relating to the biological properties of the compounds in the cited art. As was discussed in the Reply to the December 27th Office Action, none of the references cited by the Examiner teach a pharmaceutical composition or compounds with biological activities.

Furthermore, the Examiner cites other references that were not relied upon in the rejection but which also supposedly make the present invention obvious. These prior art

citations include: Ishchenko et al. *Geterotsiklicheskikh Soedinenii* 2002, 38(3), 274-280 (hereafter "Ishchenko 1"); Murti et al., *Tetrahedron Letters* 1964, 2995-2997 (hereafter, "Murti"); Kariyone et al., *Yakugaku Zasshi*1960, 80, 746-749 & 749-752 (hereafter, Kariyone); Rahatgaonkar et al., *Indian Journal of Heterocyclic Chemistry* 1996, 5, 323-324 (hereafter, "Rahatgaonkar"); Meshcheryakova et al., *Farmatsevticheskii Zhurnal* 1976, 10(3), 37-41 (hereafter, "Meshcheryakova 1"); Basinski et al., *Polish Journal of Chemistry* 1991, 65, 1619-1632 (hereafter, "Basinski"); Kostanecki et al., *Berichte der Deutschem Chemischen Gesellschaft* 1908, 41, 783-786 (hereafter, "Kostanecki"); Spatz et al., *Journal of Organic Chemistry*, 1959, 24, 1381-1382 (hereafter, "Spatz"); Lacova et al., *Molecules* 1998, 3(3), 120-131 (hereafter, "Lacova"); Ishchenko et al., *Khimiya Geterotsiklicheskikh Soedinenii* 1995, 3, 322-324 (hereafter "Ishchenko 2"); Grishko et al., *Ukrainskii Khimicheskii Zhurnal* 1985, 51(2), 211-217 (hereafter, "Grishko"); Balbi et al., *Farmaco, Edizione Scientifica* 1982, 37(6), 387-397 (hereafter, "Balbi"); Peglion et al., U. S. Patent No. 5,593,989 (hereafter, "Peglion"); Beugelmans et al., *Tetrahedron Letters* 1976, 25, 2145-2148 (hereafter, "Beugelmans"); Vorozhtsov et al., *Doklady Akademii Nauk SSSR* 1965, 164(5), 1046-1049 (hereafter, "Vorozhtsov"); Bell et al., *Australian J. of Chemistry* 1963, 16(4), 690-694 (hereafter, "Bell"); Meshcheryakova et al., *Khimiko-Farmatsevticheskii Zhurnal* 1976, 10(3), 37-41 (hereafter, "Meshcheryakova 2"); Blicke et al., *J. of Organic Chemistry* 1960, 25, 693-698 (hereafter, "Blicke"); and Aitmambetov et al., *Khimiya Prirodnykh Soedineii* 2000, 36(1), 47-50 (hereafter, "Aitmambetov"). These references teach the synthetic preparation of various flavones and related compounds. None of Ishchenko 1, Murti, Kariyone, Rahatgaonkar, Meshcheryakova 1,Basinski; Kostanecki, Spatz, Lacova, Ishchenko 2, Grishko, Balbi, Peglion, Beugelmans, Vorozhtsov, Meshcheryakova 2, Blicke, and Aitmambetov teach a pharmaceutical composition.

Therefore, neither Moon by itself or in combination with any of the above-mentioned references provides a person skilled in the art any reason to prepare the

pharmaceutical compositions of the invention. Accordingly, applicants respectfully request that the rejection of claims 47, 81, 83-85, 87-90, 92-94, 96-98, and 101 under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

Applicants request that the Examiner consider the remarks herein and allow the claims to pass to issue. Applicants also request that the Examiner rejoin and examine the non-elected subject matter of claims 52 and 53, and allow these claims to pass to issue. Should the Examiner deem expedient a telephone discussion to further the prosecution of the above application, applicants request that the undersigned be contacted at the Examiner's convenience.

Respectfully submitted,

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